Quality of life of survivors of testicular germ cell cancer

Fleer, J; Hoekstra, HJ; Sleijfer, DT; Hoekstra-Weebers, JEHM

Published in:
Supportive Care in Cancer

DOI:
10.1007/s00520-004-0646-x

Publication date:
2004

Support Care Cancer (2004) 12:476–486
DOI 10.1007/s00520-004-0646-x

REVIEW ARTICLE

J. Fleer
H. J. Hoekstra
D. Th. Sleijfer
J. E. H. M. Hoekstra-Weebers

Quality of life of survivors of testicular germ cell cancer: a review of the literature

Received: 14 January 2004
Accepted: 20 April 2004
Published online: 4 June 2004

This research was supported by a grant from the Dutch Cancer Society, no. RUG 99–2130

J. Fleer · H. J. Hoekstra (✉)
Department of Surgical Oncology,
University Hospital Groningen,
PO Box 30.001, 9700 RB Groningen,
The Netherlands
e-mail: h.j.hoekstra@chir.azg.nl
Tel.: +31-50-3612303
Fax: +31-50-3614873

D. T. Sleijfer
Department of Medical Oncology,
University Hospital Groningen,
Groningen, The Netherlands

J. E. H. M. Hoekstra-Weebers
Department of Health Psychology,
University Hospital Groningen,
Groningen, The Netherlands

J. E. H. M. Hoekstra-Weebers
Comprehensive Cancer Center
North-Netherlands,
Groningen, The Netherlands

Abstract *Goals of work:* Testicular cancer (TC) affects young men in the prime of life. The excellent prognosis and an increasing incidence have led to a growing number of testicular cancer survivors (TCSs). The aim of this review was to summarize and discuss research findings on the quality of life (QOL) of TCSs in terms of physical, psychological, and social well-being. *Patients and methods:* Literature databases were used to identify studies published between 1980 and 2003. A quality assessment using methodological and treatment-related criteria was performed to distinguish stronger- from poorer-quality studies. *Main results:* Twenty-three studies met the inclusion criteria. Quality assessment showed that seven studies were qualitatively stronger. The majority of TCSs in both stronger and poorer quality studies reported a good QOL. Prospective and retrospective studies showed that QOL after completion of treatment increased and negative consequences of TC on life decreased compared to the situation directly after diagnosis. The stronger-quality studies reported mainly on physical and psychological well-being but did not examine social well-being and the impact of treatment-related characteristics comprehensively. *Conclusions:* Both stronger- and poorer-quality studies indicate that the majority of TCSs experience a good QOL, but the shortcomings on both the methodological and content level prevent us from drawing such a conclusion. Additional research with strong designs is needed to gain clearer insight into the QOL of TCSs as a group and of individuals at risk for physical, psychological, and social problems.

Keywords Testicular cancer survivors · Quality of life · Literature review

Introduction

Men between 15 and 45 years are in the prime of life. Major issues that concern them are career, interpersonal relationships, and starting a family. Life-threatening illnesses and the possibility of dying do not fit their outlook in this period of life [28, 50]. Nevertheless, a small percentage of these men will develop the most common neoplasm in young men: testicular germ cell cancer (TC). Despite increases in incidence, TC is an uncommon disease. It accounts for approximately 1% of all malignancies in men, although the incidence varies according to geographical area and race. Compared to other malignancies, the age distribution of TC is unusual in that the incidence declines with advancing age. Since the introduction of cisplatin-based polychemotherapy in the late 1970s, (disseminated) TC has become one of the most curable malignancies [8, 14].

There are two histological types of TC: seminomatous and nonseminomatous tumors. Treatment for TC depends on histological type and stage of disease. Nowadays, treatment for stage I nonseminomatous disease consists of surgical removal of the affected testis (orchidectomy) and surveillance or nerve-sparing retroperitoneal lymph-node dissection. Initial treatment for disseminated disease (stages II–IV) is cisplatin-based polychemotherapy followed by resection of residual retroperitoneal or pulmonary tumor mass if necessary. Patients with a stage I and IIA/B seminoma are treated with orchidectomy and radiotherapy, while those with stages IIC–IV are treated with chemotherapy [8].

At present, almost 90% of testicular cancer patients can be cured with existing treatment modalities. Owing to the excellent prognosis, the young age and an increasing incidence, the number of testicular cancer survivors (TCSs) is growing. These men may have an additional life expectancy of perhaps 50 years after treatment and consequently they will have to face possible sequel of diagnosis and treatment for the rest of their lives [42]. The first reports that dealt with the quality of life (QOL, an umbrella term for physical, psychological, and social well-being) of TCSs appeared a few years after the breakthrough in medical treatment. Since that time, studies have been performed on the consequences of the experience with TC for a variety of QOL domains. Unfortunately, a critical overview of the current state of knowledge on the QOL of survivors has not been published at this point in time, while the group of survivors is growing and the literature continuous to expand. A thorough review of the literature may guide clinicians when providing patients with information on possible short- and long-term effects of the experience with TC on their lives, and it may provide insight into areas that need more research. The aims of this study were: (1) to review the literature on the QOL (physical, psychological, and social well-being) of TCSs, and (2) to assess the impact of treatment-related characteristics, such as time since diagnosis and type of treatment, on the QOL of survivors.

Patients and methods

MEDLINE, EMBASE, PsycINFO and CancerLIT databases were used to identify relevant publications, as were the references of these papers. Keywords were "testicular cancer," "testicular neoplasm," "neoplasm," "cancer," "cancer survivors," "survivors," and "quality of life." To encompass a wide range of QOL outcomes, we also used the following descriptor terms: "depression," "anxiety," "distress," "marital functioning," "social functioning", and "work-related problems." Selection criteria were: (1) papers published in English between 1980 and October 2003, (2) studies on patients with TC who were in complete remission, (3) studies on physical, psychological, and social well-being, and (4) papers in which subgroups of TCSs could be clearly identified. Operationalizations of physical, psychological, and social well-being were based on the literature on QOL in cancer survivors [3, 10, 24, 26, 32, 51]. For physical well-being, the focal points were subjective perceptions of general health, fatigue, and body image. Physical side-effects of the treatment for TC were not included because these aspects have been addressed in previous studies [8, 25, 34, 43]. For psychological well-being, distress (including anxiety and depression), health worries, and psychological well-being were chosen from the variety of possible operationalizations. In addition, distress about infertility due to treatment was evaluated. For social well-being, the focal points were marital functioning, social support, and functional life. Although sexual well-being is also an important outcome variable, it was not included, because this issue has received extensive attention recently [29, 36].

Methodological aspects were not used as an inclusion criterion, because the aim was to make an inventory of the literature on the QOL of TCSs. Studies with methodological shortcomings, such as nonstandardized questionnaires and small sample sizes, may have detected relevant and valuable (site-specific) information that strong methodological studies overlooked. These studies may be of value in providing directions for future research. However, this decision not to use methodological aspects as selection criteria may decrease the power of the findings in the current study [31]. Therefore, it was decided to assess the quality of the studies first. There is no gold standard to determine which criteria should be used in quality assessments [2], but one critical issue is the internal validity of the studies, which is derived from study procedures and design. Furthermore, with regard to the research questions of this review, we considered treatment-related aspects to be important criteria as well. Therefore, the following methodological and treatment-related aspects were used for quality assessment: design, sample size, use of comparison groups, measurement instruments, type of treatment, and time since diagnosis.

It needs to be pointed out that results of individual studies involving comparison of groups or correlational analyses are only reported when they were statistically significant at a level of $p \leq 0.05$ in the analyses.

Results

A total of 23 studies met the inclusion criteria. Table 1 shows the data on the aspects that were considered in the quality assessment. Quality assessment revealed that studies differed greatly in quality. Seven studies were considered as stronger [19, 20, 27, 40, 41, 42, 47], because on the whole, these studies used suitable designs, had adequate sample sizes, used validated questionnaires and comparison groups (with exception of the two prospective studies) [20, 47], and had large ranges in time since treatment (with exception of the two prospective studies). Furthermore, these studies considered time since treatment in their analyses, whereas in total, only nine studies investigated whether time since diagnosis was related to one of the outcome variables [7, 11, 16, 19, 27, 35, 39, 40, 41]. None of these studies found a relationship between time since diagnosis and any of the dimensions of QOL. Five of the qualitatively stronger studies were published recently (between 2000 and 2003). However, the remaining two stronger studies were published in 1989, indicating that the poorer-quality studies were not necessarily the earlier studies.

Because it is probable that the findings from the stronger-quality studies will have more power and would

Table 1 Studies included in this review (alphabetical order) and information on criteria used for quality assessment. *CT*: chemotherapy; *RT*: radiotherapy; *RRTM*: resection of residual tumor mass (including retroperitoneal lymph node dissection and resection of pulmonary tumor mass); *M*: mean; *n.r.*: not reported in publication; *SWL*: Satisfaction with Life; *POMS*: Profile of Mood States; *CES-D*: Centre for Epidemiological Studies-Depression Scale; *SAS*: Social Activities Scale; *CPBS*: Cancer Patient Behavior Scale; *BMS*: Brannon Masculinity Scale; *EORTC QLQ-C30*: European Organization for Research and Treatment Quality of Life Questionnaire-C30: *IES*: Impact of Events Scale; *GHQ-28*: General Health Questionnaire-28; *HADS*: Hospital Anxiety and Depression Scale; *FQ*: Fatigue Questionnaire; *OLQ*: Orientation to Life Questionnaire; *FES*: Family Environment Scale; *SF-36*: Medical Outcome Study 36-item Short Form Health Survey; *HSCL*: Hopkin Symptom Checklist; *PSE*: Present State Examination; *SWEDQUAL*: Swedish Health Related Quality of Life Questionnaire; *GQL*: Gothenburg Quality of Life Instrument

Study + design	Subjects	Age at time of data collection	Measurement instruments	Disease stage	Treatment in addition to orchidectomy	Time since diagnosis
	(*n*)	(years)		(%)	(%)	(years)
Arai et al. (1996) [4] Retrospective	83	18–60, median=33.8	SWL (validated); self-developed and translated questions, based on Stuart et al. 1990 [46]; Kaasa et al. 1991 [30]; Aaronson et al. 1987 [1] (psychometric qualities n.r.)	I=57.8 II=19.3 III=22.9	Surveillance= 8.4 R=50.6 CT±RRTM=41	1–21.8, median=8.0
Bloom et al. (1988) [6], (1993) [7] Retrospective	Testicular: see Gritz et al. [21] Control: 85	See Gritz et al. [21] Control: median=28	Bloom et al. (1988, 1993): work-related questions developed by Barofsky (1978) [5] (psychometric qualities n.r.) Bloom et al. (1993): POMS and CES-D (standardized questionnaires, proven psychometric qualities), SAS (psychometric qualities n.r.), self-developed questions (psychometric qualities not assessed)	See Gritz et al. [21]	See Gritz et al. [21]	See Gritz et al. [21] Control: median=3
Brodsky (1995) [9] Retrospective	Nonseminoma: 11	median=35	Qualitative interview with open-ended questions	n.r.	n.r.	>3 after treatment
Caffo et al. (2001) [11] Retrospective	Seminoma: 98	26–85, median=48	Self-developed questionnaire (validated)	n.r.	RT=100	1.25–36, median=10.3 after treatment
Cassileth & Steinfeld (1986) [12] Cross-sectional	Seminoma: 39 Control: 39	Seminoma: 22–67, median=41.0 Control: 25–75, median=42.9	POMS; self-developed questions (psychometric qualities n.r.)	I=65 >I=35	RT=100	1–20, median=7.3
Douchez et al. (1993) [15] Retrospective	Nonseminoma: 109 Control:107	Nonseminoma: 24–66, median=39.4 Control: age-matched	Self-developed questions (psychometric qualities n.r.)	I=53.2 II=39.5 III=7.3	RRTM=3.7 RT+CT=9.2 RT±RRTM=4.6 CT±RRTM=65.1 RT+CT+RRTM=17.4	median=9.1
Edbril & Rieker (1989) [16], Rieker et al. (1985) [39] Cross-sectional	74	19–59, median=30	POMS; CPBS (abbreviated; psychometric qualities n.r.); BMS; self-developed questions (psychometric qualities n.r.)	n.r.	RT=8 CT=27 RRTM=16 RT+CT+RRTM=50	2–10, median=4 after treatment
Fossa et al. (1999) [18] Cross-sectional	Bilateral: 43	31–75, median=41	EORTC QLQ C-30; IES; GHQ-28 (standardized questionnaires, proven psychometric qualities)	1st-2nd orchidectomy I=74.4–81.5 II=9.3–11.6 III=7–2.3 IV=9.3–4.7	1st-2nd orchidectomy Surveillance =16.3–67.8 RT=58.1–18.6 RRTM=11.6–0 CT±others=14–18.6	n.r.
Fossa et al. (2003) [20] Prospective	666	16–63, median=31	EORTC QLQ C-30 + TC module	>I	CT=100%	After orchidectomy, 3 months, 6 months, 1 year, 2 years
Fossa et al. (2003) [19] Cross-sectional	Testicular: 791 Control 1: 706 Control 2: 27083	Testicular: 23–75, median=44 Control 1: <75 Control 2:19–74	HADS; FQ (standardized questionnaires, proven psychometric qualities)	n.r.	Surveillance±RRTM=20 RT=41 CT±others=39	4–21, median=12
Gritz et al. (1988) [21] Cross-sectional	88	18–60, median=35.2	POMS; CES-D; self-developed questions (psychometric qualities n.r.)	I=48 II=37 III=15	RT=42 CT=47 RRTM=50	1–7.5, median=3.8 after treatment
Gritz et al. (1990) [22] Cross-sectional	34	median=37.7	POMS; CES-D; OLQ (sense of coherence); FES (standardized questionnaires, proven psychometric qualities)	n.r.	Surveillance=2.9 RT=44.1 CT=8.8 RRTM=20.6 RT+CT=2.9 CT+RRTM=20.6	1–7.5, median=4 after treatment
Joly et al. (2002) [27] Case-control	Testicular: 71 Control: 119	Testicular: 29–67, median=47 Control: 29–67, median=48	EORTC QLQ C-30; SF-36 (standardized questionnaire, proven psychometric qualities)	I=64.8 >I=35.2	Surveillance=9 RT=48.2 CT±RRTM=36.8 RT+CT=5.9 RRTM=19.7	5–20, median=11

Table 1 (continued)

Study + design	Subjects	Age at time of data collection	Measurement instruments	Disease stage	Treatment in addition to orchidectomy	Time since diagnosis
	(*n*)	(years)		(%)	(%)	(years)
Kaasa et al. (1991) [30] Cross-sectional	Testicular: 149 Control 1: 6277 Control 2: 1638 Control 3: 520	Testicular: 17–64, median=34 Control groups: age-matched	HSCL (standardized questionnaire, proven psychometric qualities); self-developed questions (psychometric qualities n.r.)	median=2 I=51 II=32.2 III=2.7 IV=12.1	RT=26.2 RRTM=21.5 CT+RRTM=30.8 CT+RT±RRTM=21.5	Total: 3–9, median=5.1
Moynihan (1987) [35] Retrospective	97	15->40	PSE (standardized instrument)	I=43.1 >I=56.9	Surveillance=19 RT=4 CT=5 RT+CT=31 CT+surgery=29 RT+CT+surgery=12	Up to 5
Ozen et al. (1998) [37] Cross-sectional	140	18–51, median=32	GHQ-28; self-developed questions (psychometric qualities n.r.)	I=43.6 II=40 III=3.6 IV=12.8	Surveillance=15.7 RT=16.4 CT=48.6 RT+CT=2.9 CT+post-CT surgery=16.4	1.2–8, median=4.5
Rieker et al. (1989) [40] Retrospective	Testicular: 223 Control: 120	Testicular: 17–65, median=33 Control: 19–60, median=30.5	See Edbril and Rieker (1989) and Rieker et al. (1985)	I=32 >I=68	RT=32 CT=9 RRTM=17 CT+RRTM=33 RT+surgery±CT=9	<2:18 2–5: 51 ≥6: 32
Rudberg et al. (2000) [41] Retrospective	Testicular: 277 Control: 122	Testicular: 18–83, median=42.2 Control: 25–54, median=39	SWEDQUAL (standardized questionnaire, proven psychometric qualities); self-developed questions (psychometric qualities n.r.)	I=45.1 >I=54.9	Surveillance=8 RT=37.1 CT=9.8 RRTM=11.9 CT+RRTM=27.8 RT+CT±RRTM =5.4	3–13, median=7.8
Rudberg et al. (2002) [42] Retrospective	Testicular: 277 Control: 392	Testicular: 18–83, median=42.2 Control: median=45	GQL (only symptom checklist; reliable, validity n.r.); self-developed questions (psychometric qualities n.r.)	See Rudberg et al. [41]	See Rudberg et al. [41]	See Rudberg et al. [41]
Stuart et al. (1990) [46] Retrospective	62	CT: 19–48, median=29 RT: 20–48, median=33	Self-developed questions (psychometric qualities n.r.)	I/IIA=74.2 IIB/C=11.3 III=3.2 IV=11.3	RT=54.8 CT=45.2	CT: 0.5–2.7, median=2.7 after treatment RT: 0.6–5.6, median=2.4 after treatment
Tamburini et al. (1989) [47] Prospective	31	18–50, median=29.3	Spitzer QL index (standardized questionnaire, proven psychometric qualities); self-developed questions (psychometric qualities n.r.)	I=16.1 >I=83.9	RT=16.1 CT=41.9 RRTM=19.4 CT+surgery=22.6	0.25, 0.5 and 1.5

best answer the research questions of this review, it was decided to discuss the results of these studies first. The results of the remaining studies will be related to these seven studies, and possible differences in results will be explained using the quality criteria.

One last remark should be made about type of treatment. Eight retrospective/cross-sectional studies included both TCSs that had been treated before and after 1978 (when cisplatin-based chemotherapy was introduced) [4, 11, 12, 16, 18, 35, 39, 40]. However, it was not possible to compare the two time periods, because the studies did not consider changes due to developments in treatment in their analyses. Furthermore, most studies only considered treatment-related characteristics as independent variables. Other factors that could possibly influence the outcome, such as sociodemographic characteristics and the patient's support system, were usually not considered. All factors reported on by the studies that have a significant effect on the outcome variable are reported in the current review.

Physical well-being

Health perception

Four of the qualitatively stronger studies reported on health perception. Prospectively, it was shown that physical functioning of TCSs treated with chemotherapy recovered to baseline levels during the 2 years following diagnosis [20]. At time of study, over 70% of TCSs assessed their general health as good [41], and perceived their health and physical functioning as equal to that of age-matched healthy men [27, 41]. None of these qualitatively stronger studies compared treatment groups.

The poorer-quality studies reported comparable findings. Several studies reported that TCSs experienced no change in health status compared to the pretreatment situation, and between 63 and 90% assessed their general health as good [4, 7, 11, 21, 46]. Two studies found no differences in perceived health and physical functioning between TCSs and age-matched healthy men or men treated for Hodgkin's disease [7, 15]. However, one study that did not use a validated questionnaire reported that TCSs assessed their own health as better than that of controls [30]. No differences in physical well-being were found between men treated with different treatment modalities [4, 30, 46].

Fatigue

Fatigue was studied relatively comprehensively by the qualitatively stronger studies. Prospectively, an improvement of fatigue was reported in TCSs treated with chemotherapy, although 19% experienced deterioration in fatigue 2 years after treatment [41]. Eighty-four percent experienced no chronic fatigue at time of study [19]. Two studies found that fatigue scores did not differ from those of age-matched healthy men or the general population [27, 42], but Fossa et al. [19] reported that TCSs younger than 30 years experienced more fatigue than the same age cohort of the general population. Furthermore, it was found that TCSs who experienced more fatigue reported a poorer overall QOL [27]. Fatigue was associated with pretreatment distress, morbidity, lower educational level, older age, comorbidity, and higher levels of depression and anxiety [19]. Differences between treatment groups were not found [19, 27].

Overall, results of the poorer-quality studies were in line with those of the qualitatively stronger studies. Two studies reported that most TCSs felt energetic (75% [21] and 82% [11]), although it took an average of 9 months for energy levels to return to normal [21]. Compared to men treated for Hodgkin's disease, energy levels returned to normal in more TCSs, and they reported less fatigue at the time of data collection [7, 18]. Fatigue scores of TCSs did not differ from those of norm groups or age-matched healthy men [21, 22, 39]. In contrast with the qualitatively stronger studies, one study reported that men treated for seminoma experienced more fatigue than men treated for nonseminoma [21], but this last study had a much smaller sample size than the stronger studies [19, 27].

Body image

The loss of a testicle, which is an organ associated with masculinity and sexuality, may result in an impaired body image [49]. The body image of TCSs returned to normal in the course of time, and at the time of data collection, most TCSs in the qualitatively strong studies did not report feeling less attractive (77.3% [42] and 84.8% [41]) or less masculine than before TC (79%) [20]. Men who felt less attractive had lower scores in most health-related QOL domains, reported more fatigue, and were less satisfied with their family life than those who did not feel less attractive [41, 42]. These results were supported by the poorer-quality studies, which found that the majority of TCSs had no changed body image (56–94%) [7, 9, 11, 35]. In addition, these studies reported that the body image of TCSs did not differ from that of men treated for Hodgkin's disease, and their feelings of masculinity were equal to those of sociodemographically matched men [7, 12]. None of the reviewed studies compared treatment modalities.

Psychological well-being

Psychological distress

In the qualitatively stronger studies, the levels of psychological distress experienced by TCSs varied between 9 and 27% [19, 40, 41]. One of these studies reported that TCSs as a group experienced significantly less distress than controls [40]. However, Fossa et al. [20] found that TCSs experienced more anxiety but less depression than the general population. One study found that a quarter of the TCSs became more anxious after diagnosis and treatment [40]. The contradictory results may be explained by the different aspects of distress addressed in these studies and the use of different validated questionnaires. None of the qualitatively stronger studies compared treatment modalities.

A study of poorer quality reported that 13% of the TCSs experienced depression and 16% tension [11]. In retrospect, TCSs reported more anxiety, depression, and distress during the first 6 months after diagnosis than male college students, but levels decreased over time [15, 21, 30, 35]. One study stated that scores did not return to baseline levels, another study found that 12 months after diagnosis, TCSs treated with radiotherapy experienced less distress than male college students [11, 15]. A significant number of TCSs experienced more depression since treatment [4]. Partly in contrast with the results of Fossa et al. [20], two poorer-quality studies using self-developed questionnaires reported that TCSs experienced more anxiety, depression, and psychosocial problems than age-matched men and controls [15, 30]. Furthermore, three studies using validated questionnaires but small sample sizes found no differences in levels of anxiety and depression between TCSs and age-matched men, psychiatric patients, male college students, and other cancer patients [21, 22, 39]. In line with Rieker et al. [40], two studies reported that TCSs experienced less distress than healthy sociodemographically matched men, male college students, and psychotherapy patients [7, 21]. In addition, one study found that men treated with radiotherapy reported more depression, but two other studies showed no differences between treatment groups [4, 30, 46]. The small sample sizes of the different treatment groups and the use of self-developed questionnaires may explain these contradictory results.

Health worries

Seventeen percent of the TCSs in the qualitatively stronger study of Fossa et al. [20] reported an increase of fear of recurrence 2 years after baseline measurement, whereas anxiety had decreased in 36%. Since their experience with TC, 19% of TCSs reported more fear of dying, while 32% reported less fear [40]. None of the stronger studies reported on differences between treatment modalities in health worries.

In concurrence with Fossa et al. [20], decreases in fear of recurrence (from 45 to 12%) and in fear of developing a second primary malignancy (from 50 to 21%) were reported in the poorer-quality studies, although health worries were still present in 54–76% of TCSs [4, 18, 21, 35, 46]. TCSs who reported more anxiety and depression were more afraid of a tumor recurrence, spent more time worrying about their health, and had more concerns about their health [35]. One study found no differences in health worries between men who received different treatment modalities; a second study reported that radiotherapy patients worried more about their health after treatment; a third study showed that men treated with chemotherapy experienced greater fear of a tumor recurrence than men treated with radiotherapy [4, 21, 46]. As mentioned earlier, a likely explanation for the contradictory results between studies that compared treatment groups are the small sample sizes and the use of nonvalidated questionnaires to assess health worries.

Fertility distress

TC strikes men at an age when fertility is a major concern. Cancer-treatment modalities are known to result in infertility [7]. Prospectively, it was found that fertility distress decreased during the 2 years after treatment in 28% of TCSs, but it increased in 11% [20]. Compared to sociodemographically matched healthy men, TCSs reported more overall problems with being infertile (5% compared to 22%) [40]. Infertility distress was reported most by TCSs with posttreatment ejaculatory dysfunction, those without children, of younger age, with a lower income, and those treated with chemotherapy and retroperitoneal lymph-node dissection (RPLND) [39, 40]. Across the treatment groups, percentages of fertility distress varied from 11% in the radiotherapy group to 33% in the men treated with chemotherapy and RPLND [40].

The poorer-quality studies reported that during and after treatment, TCSs were more anxious about infertility than before diagnosis, but men who were infertile and those who were uncertain about their fertility status were not significantly more depressed and anxious than those who were fertile [35, 37]. The majority of the 11 TCSs that were interviewed reported discomfort and regret about possible infertility [9]. Only one study reported on fertility distress in men treated for bilateral TC. Surprisingly, these men reported few problems with their fertility status, but the sample size was small and the study used one question only to assess fertility distress [18].

Psychological well-being

Although many QOL studies have shown that cancer and its treatment have detrimental effects on patient's lives, there is a growing awareness that there may also be positive effects. The prospective studies showed that the QOL of TCSs improved progressively after orchidectomy or chemotherapy [20, 47]. At time of study, TCSs and age-matched men reported a similar QOL, and there were no differences between treatment modalities [27].

The results of the poorer-quality studies were rather positive as well. One study found that TCSs reported being more satisfied with their lives than age-matched men [30], and two studies reported a similar QOL in TCSs, and norm-group men, and controls [12, 18]. Over 73% of TCSs experienced good QOL after treatment [11]. A positive rather than negative impact was experienced by over half of the TCSs (exact percentages unknown), while 76% considered that surviving cancer was a worthwhile achievement [39]. Several positive effects were mentioned, including the ability to enjoy oneself, renewed appreciation of life, emotional growth, and the resetting of priorities and values [9, 39]. The experience of cancer benefited the psychological well-being of most patients treated with chemotherapy (77%) and radiotherapy (82%) [46]. In one study, men treated with radiotherapy or chemotherapy reported greater satisfaction with life than men in the surveillance group, but this result was not confirmed by another study [4, 30]. Again, a probable explanation for the contradictory results are the small samples and the use of self-developed questionnaires.

Social well-being

Marital functioning

Treatment for TC is known to have repercussions on marital functioning [23]. The qualitatively stronger studies reported that most TCSs did not experience a change in the relationship with their partner after their experience with TC [40, 41] and that treatment groups did not differ in their responses to questions about changes in the partner relationship since treatment [47].

The subject of marital functioning received much more attention in the poorer-quality studies. Quite similar to the results of the stronger studies, most of TCSs in these studies reported that the relationship with their partner had not changed or had become stronger after their experience with TC [4, 9, 35, 46]. Anxiety about separation from the spouse was not a concern before, during, or after treatment in most TCSs (84–94%), while scores on spouse importance and quality of communication did not differ over the course of time. The degree of support from the spouse increased during treatment as compared to the situation prior to diagnosis and decreased again afterwards [37]. In TCSs, of patients who experienced a change in their partner relationship after TC, most married men indicated that the relationship had strengthened (68%), whereas 74% of unmarried men reported that it had become strained [39]. TCSs appeared to be more satisfied with their partner relationship than sociodemographically matched men [12]. Treatment groups did not differ in their responses to questions about changes in partner relationships since treatment, although men treated with the most extensive treatment modality (radiotherapy, chemotherapy, and/or RPLND) reported less satisfaction with family life than the other treatment groups [4]. This finding was in line with the qualitatively stronger study.

Single TCSs may have difficulties starting a relationship not only on account of the above-mentioned issues with infertility, sexual functioning, and altered body image, but also due to the feeling of estrangement from their peers without a history of cancer. No qualitatively stronger study considered this issue, and only one poorer-quality study reported on TCSs who were not involved with a partner or were not married at the time of their diagnosis and treatment. This study showed that two out of the ten patients who got married after treatment found that having had TC caused difficulties in the marital process, while 35% of the 28 men who were single at the time of data collection thought that the cancer experience would form a problem in planning a marriage [37].

Social support

Only one qualitatively stronger study focussed on social functioning after TC. This study reported that TCSs experienced fewer changes in relationships with friends than sociodemographically matched healthy men [27]. The qualitatively poorer studies showed that the experience of TC did not result in changed relationships with family (66–93%) and friends (77–95%) [4, 11, 46]. Furthermore, it was reported that 92% of TCSs were satisfied with the support they received during treatment [35]. They mentioned more "enriching" relationships with family and friends, although they had become more selective [9]. One study showed no differences between treatment groups, but another study reported improved relationships with family and friends in patients treated with chemotherapy [4, 46].

Functional life

Long-term side-effects of treatment (such as fatigue, psychosocial problems, and fear of tumor recurrence), may cause difficulties in resuming work or study after treatment [17]. The qualitatively stronger studies reported that at the time of data collection, 76–90% of TCSs were employed [27, 40, 41] and that their employment status

was no different from that of age-matched healthy men [27]. Furthermore, Joly et al. [27] reported that TCSs and controls had similar problems in their professional lives, although TCSs were less ambitious than controls.

The poorer-quality studies reported more extensively on functional life. These studies also showed that most TCSs were employed at the time of data collection (82–98%) [6, 7, 16, 35, 39]. Their employment status after treatment appeared to be the same as before [11, 16, 39, 46], and it was better than that of men treated for Hodgkin's disease [6]. Over 90% of TCSs who returned to work perceived no effect on their career mobility, 45% experienced no effect on their ambition and career plans (while 26% reported a positive effect), and 52% experienced no effect on their satisfaction with work (while 32% reported more satisfaction) [39]. In line with the results of Joly et al. [27], two studies found that work and ambition had become less important since TC, because men had reorganized their priorities and had adopted a new philosophy of working to live rather than living to work [9, 16]. Compared to men treated for Hodgkin's disease, TCSs were better able to work at their former pace [7]. Compared to age-matched controls, TCSs felt less physically exhausted after a working day and could maintain significantly better concentration and attention at work [30].

Small percentages of TCSs reported negative effects of the cancer treatment on their work satisfaction (16%), career mobility (10%), ambitions and career planning (29%), and relationships with supervisors and coworkers (5–14%), while 12–25% were unable to work at their former pace, finish tasks, and had problems with concentration [6, 7, 16, 39]. In terms of treatment groups, between 12–31% of men treated with radiotherapy or chemotherapy reported job loss and loss of job prospects because of their illness [4, 46]. Deterioration in professional performance was reported by 17% of the radiotherapy group and 3% of the other treatment modalities [37]. Men in the surveillance group were less comfortable with their work than TCSs treated with chemotherapy or radiotherapy and had more problems with concentration and attention at work than TCSs treated with chemotherapy. However, another study found no differences between treatment groups [4, 30]. Men treated with radiotherapy were more satisfied with their work than those treated with chemotherapy or those in the surveillance group, and they felt that work was more worthwhile than those in the surveillance group [4]. There was no difference between treatment groups with respect to physical exhaustion after work [4, 30]. All of these poorer quality studies had serious methodological shortcomings: sample sizes of the total groups (only two studies included more than 100 TCSs) and the treatment groups were small, all studies used nonvalidated questionnaires or questionnaires of which the psychometric qualities were not reported, and no study compared TCSs with sociodemographically matched healthy men.

Discussion

The goal of this study was to give a comprehensive review of the literature of primary studies examining physical, psychological, and social well-being of TCSs. A total of 23 studies, published between 1985 and 2003, met the inclusion criteria. Because these studies used such a broad variety of methodologies and research questions, this review was by necessity descriptive. However, a quality assessment was performed to interpret and explain contradictory results and to increase the power of this review. Based on methodological and treatment-related criteria, seven studies appeared to be qualitatively stronger.

Results of both stronger- and poorer-quality studies appeared quite similar. Prospective and retrospective studies showed that QOL after completion of treatment increased and that the negative consequences of TC on life decreased compared to the situation directly after diagnosis when a poorer QOL was observed. For example, energy levels returned to normal, fatigue decreased, and TCSs became used to their changed body image. Decreases were found in psychological distress, anxiety, depression, and fear of tumor recurrence. The stronger-quality studies paid little attention to social dimension (marital functioning, social support, and functional life) and positive effects of the experience with TC. Poorer-quality studies reported that, besides a decrease in negative consequences of TC on the patients' lives, the experience of TC seemed to have positive effects. A considerable proportion of TCSs reported that they experienced emotional growth, were appreciating life more, and had stronger relationships with family and friends. Results on functional life were mainly contradictory.

Based on this summary of the results, one could assume that in general, TCSs experience a good QOL. However, this could be an arguable assumption because of the methodological shortcomings of most studies and because the stronger-quality studies did not investigate all dimensions of QOL with the same extensiveness. Below we discuss various methodological issues.

Firstly, many studies used a retrospective design to evaluate the well-being of TCSs and to compare their well-being before and/or after treatment. Data obtained in retrospect are less reliable for two reasons: (1) the chance is great that recall was distorted (selective memory bias), because 1–36 years had passed between data collection and diagnosis [13, 31, 39, 41]; (2) under the influence of certain life events (such as experience with cancer), internal standards can change (response shift) and cause people to evaluate new situations according to other standards [44]. For example, people can become accustomed to a higher level of fatigue, and after a certain

amount of time, report the same QOL as that prior to the illness [38, 45]. Such changes in internal standards cannot be reproduced accurately in retrospective studies. The only way that conclusions can be drawn from cross-sectional or retrospective studies about the relationship between TC and QOL is to compare the current QOL of TCSs to that of a sociodemographically-matched group.

Secondly, a considerable number of studies had no comparison group. Some studies used norm groups, but these often differed from TC patients in sociodemographic areas. In studies that compared TCSs to other cancer patients, it often appeared that the other cancer patients had a poorer prognosis and had received other forms of treatment.

Thirdly, a wide variety of both validated and nonvalidated measurement instruments were used to evaluate the same aspects of QOL, which made it difficult to compare results. Therefore, some differences in findings may be due to the different instruments that were used, even if they were validated measures. In studies that used nonvalidated instruments, some variables (e.g., body image) were measured with only one or two items. This affected the reliability of study results, and it is not clear whether their scope is of sufficient depth [33].

Fourthly, descriptive and comparison analysis methods were generally used, whereas techniques such as regression analyses would have enabled the identification of possible risk groups.

Fifthly, in a large proportion of the studies, reliability and generalizability were affected by small numbers (fewer than 100 TCSs). A small study group means that there is insufficient power to determine the possible influence of demographic and treatment-related variables [27].

Sixthly, the majority of studies did not correct for confounding variables such as age, marital status, education level, time since diagnosis, treatment modality, and disease stage, although they aimed to measure the negative impact of illness or treatment on QOL. To identify possible groups of men who are at risk of developing problems, it is essential to control for demographic and treatment-related variables.

In addition to these methodological issues, the studies showed limitations in how they applied the treatment-related variables. Only nine studies considered time since diagnosis in their analyses, and the categorizations of treatment modalities were rough. None of the studies reflected on changes in treatment over time, which may have caused a threat to the internal validity.

From a historical point of view, the differences in methodologies between studies and the methodological shortcomings of most studies are well explainable. The earlier studies had to use explorative designs, self-developed, and nonvalidated questionnaires and could only focus on short-term sequel of survivorship. In contrast, the more recent studies could make use of well-validated and reliable instruments developed over the years. Furthermore, the number of survivors has greatly increased due to advances in medical treatment, making methodologically stronger studies possible. Therefore, it was not surprising that five of the seven methodologically stronger studies were published between 2000 and 2003, although the poorer-quality studies were not necessarily the earlier studies.

A problem of studies with methodological shortcomings is that their results may not always concur with reality. This can be illustrated with three examples from this review. Firstly, it would have been reasonable to expect that more extensive treatment would cause more short- and long-term physical and psychosocial side effects. It may be that the lack of documented effect of treatment reflects inadequate methodology, lack of adequately powered and comprehensive studies, and the rough categorizations of treatment modalities. A second example that illustrates the distorting effect of methodological shortcomings on the outcomes of this review is the wide variety of percentages between studies of TCSs reporting negative effects. For example, the level of psychological distress varied between 8% and 27%, while 5% to 29% were experiencing work-related problems since TC. A third example is the result that men with bilateral TC have less fertility issues. There is only one study that states this, and given the lack of biological rationale for this observation, it may be regarded as casuistry and not as a reflection of reality.

As regard to content, more research is needed as well. The qualitatively stronger studies did not exhaustively delve into any of the outcome variables, indicating that more research is needed on all dimensions of QOL but most of all in the area of social well-being and the impact of treatment-related characteristics. The poorer-quality studies provided some directions for future research. In particular, issues that may be of major concern for young men dealing with the sequel of cancer diagnosis and treatment, such as body image, fertility issues, intimate relationships, social support, and work-related issues, need more attention. Surprisingly few studies attacked these issues, and all these studies suffered from methodological shortcomings (nonvalidated questionnaires and small sample sizes). For example, the effects of TC on casual relationships and on men who had no partner at the — time of TC have received very little attention. One study showed that TC had a negative effect on casual relationships, whereas the relationship of many married men with their spouse became stronger. The only study that investigated whether men who were single at the time of diagnosis experienced problems with starting a new relationship found that 20% of men reported problems. It would seem worthwhile to conduct more research into the effects of TC on casual relationships and on single men, because TC particularly affects young men who are more

likely to be single or have a relationship without being married.

Future directives

In conclusion, because of the above-mentioned methodological shortcomings, it would not be justified to provide a general conclusion on the QOL of TCSs. In order to obtain such data and to gain clearer insight into the impact of TC on later QOL, more methodological strong, cross-sectional, and prospective research is needed. The studies should include large groups of patients and sociodemographically matched comparison groups, and the analyses should aim to identify subgroups that are at risk of developing psychosocial problems. To identify risk groups, it is necessary to establish the predictive value of, for example, demographic variables (age, marital status, education level), treatment-related variables (treatment modalities, time since diagnosis, disease stage, experience of a new cancer event), social support, and personality factors. In addition, on a content level, future research should pay more attention to body image, fertility distress, issues concerning intimate relationships, social support, and work-related problems. Furthermore, more attention should be paid to possible long-term side-effects of treatment with radiotherapy or chemotherapy, such as an increased risk of secondary leukemia, second primary malignancies, decreased renal functioning, hearing deficits, and cardiovascular disease [34, 48]. As knowledge of the long-term side-effects of cancer treatment has only started to increase fairly recently, very little research has been performed as yet into their possible impact on QOL.

References

1. Aaronson NK, Bakker W, Stewart AL, van Dam FS, van Zandwijk N, Yarnold JR, Kirkpatrick A (1987) Multi-dimensional approach to the measurement of quality of life in cancer clinical trials. In: Aaronson NK, Beckman J (eds) The quality of life of cancer patients. Raven Press, New York, p 63
2. Alderson P, Green SE (2003) Cochrane Collaboration open learning material for reviewers. http://www.cochrane-net.org/openlearning/. Cited 1 Nov 2003
3. Alter CL, Pelcovitz D, Axelrod A, Goldenberg B, Harris H, Meyers B, Grobois B, Mandel F, Septimus A, Kaplan S (1996) Identification of PTSD in cancer survivors. Psychosomatics 37:137–143
4. Arai Y, Kawakita M, Hida S, Terachi T, Okada Y, Yoshida O (1996) Psychosocial aspects in long-term survivors of testicular cancer. J Urol 155:574–578
5. Barofsky I (1978) Compliance, adherence and the therapeutic alliance: Steps in the development of self-care. Soc Sci Med 12:369–376
6. Bloom JR, Hoppe RT, Fobair P, Cox RS, Varghese A, Spiegel D (1988) Effects of treatment on the work experience on long-term survivors of Hodgkin's disease. J Psychosoc Oncol 6:65–80
7. Bloom JR, Fobair P, Gritz E, Wellisch D, Spiegel D, Varghese A, Hoppe R (1993) Psychosocial outcomes of cancer: a comparative analysis of Hodgkin's disease and testicular cancer. J Clin Oncol 11:979–988
8. Bosl GJ, Motzer RJ (1997) Testicular germ-cell cancer. N Engl J Med 337:242–253
9. Brodsky MS (1995) Testicular cancer survivors' impressions of the impact of the disease on their lives. Qual Life Res 5:78–96
10. Bush NE, Haberman M, Donaldson G, Sullivan KM (1995) Quality of life of 125 adults surviving 6–18 years after bone marrow transplantation. Soc Sci Med 40:479–490
11. Caffo O, Amichetti M, Tomio L, Galligioni E (2001) Quality of life after radiotherapy for early-stage testicular seminoma. Radiother Oncol 59:13–20
12. Cassileth BR, Steinfeld AD (1987) Psychological preparation of the patient and family. Cancer 60:547–552
13. de Haes J, Curran D, Young T, Bottomley A, Flechtner H, Aaronson N, Blazeby J, Bjordal K, Brandberg Y, Greimel E, Maher J, Sprangers M, Cull A (2000) Quality of life evaluation in oncological clinical trials. Eur J Cancer 36:821–825
14. Dearnaley D, Huddart R, Horwich A (2001) Regular review: Managing testicular cancer. BMJ 322:1583–1588
15. Douchez J, Droz JP, Desclaux B, Allain Y, Fargeot P, Caty A, Charrot P (1993) Quality of life in long-term survivors of nonseminomatous germ cell testicular tumors. J Urol 149:498–501
16. Edbril SD, Rieker PR (1989) The impact of testicular cancer on the work lives of survivors. J Psychosoc Oncol 7:17–29
17. Fobair P, Hoppe RT, Bloom J, Cox R, Varghese A, Spiegel D (1986) Psychosocial problems among survivors of Hodgkin's disease. J Clin Oncol 4:805–814
18. Fossa SD, Opjordsmoen S, Haug E (1999) Androgen replacement and quality of life in patients treated for bilateral testicular cancer. Eur J Cancer 35:1220–1225
19. Fossa SD, Dahl AA, Loge JH (2003) Fatigue, anxiety, and depression in long-term survivors of testicular cancer. J Clin Oncol 21:1249–1254
20. Fossa SD, de Wit R, Roberts JT, Wilkinson PM, de Mulder PH, Mead GM, Cook P, de Prijck L, Stenning S, Aaronson NK, Bottomley A, Collette L (2003) Quality of life in good prognosis patients with metastatic germ cell cancer: a prospective study of the European Organization for Research and Treatment of Cancer Genitourinary Group/Medical Research Council Testicular Cancer Study Group (30941/TE20). J Clin Oncol 21:1107–1118
21. Gritz ER, Wellisch DK, Landsverk JA (1988) Psychosocial sequelae in long-term survivors of testicular cancer. J Psychosoc Oncol 6:41–63
22. Gritz ER, Wellisch DK, Siau J, Wang HJ (1990) Long-term effects of testicular cancer on marital relationships. Psychosomatics 31:301–312
23. Hannah MT, Gritz ER, Wellisch DK, Fobair P, Hoppe RT, Bloom JR, Sun G, Varghese A, Cosgrove MD, Spiegel D (1992) Changes in marital and sexual functioning in long-term survivors and their spouses: testicular cancer versus Hodgkin's disease. Psychooncology 1:89–103

24. Holzner B, Kemmler G, Kopp M, Moschen R, Schweigkofler H, Dunser M, Margreiter R, Fleischhacker WW, Sperner-Unterweger B (2001) Quality of life in breast cancer patients–not enough attention for long-term survivors? Psychosomatics 42:117–123
25. Horwich A, Huddart R, Dearnaley D (1998) Markers and management of germ-cell tumours of the testes. Lancet 352:1535–1538
26. Joly F, Henry-Amar M, Arveux P, Reman O, Tanguy A, Peny AM, Lebailly P, Mace-Lesec'h J, Vie B, Genot JY, Busson A, Troussard X, Leporrier M (1996) Late psychosocial sequelae in Hodgkin's disease survivors: a French population-based case-control study. J Clin Oncol 14:2444–2453
27. Joly F, Heron JF, Kalusinski L, Bottet P, Brune D, Allouache N, Mace-Lesec'h J, Couette JE, Peny J, Henry-Amar M (2002) Quality of life in long-term survivors of testicular cancer: a population-based case-control study. J Clin Oncol 20:73–80
28. Jones GY, Payne S (2000) Searching for safety signals: The experience of medical surveillance amongst men with testicular teratomas. Psychooncology 9:385–394
29. Jonker-Pool G, van de Wiel HB, Hoekstra HJ, Sleijfer DT, van Driel MF, van Basten JP, Schraffordt Koops HS (2001) Sexual functioning after treatment for testicular cancer–review and meta-analysis of 36 empirical studies between 1975–2000. Arch Sex Behav 30:55–74
30. Kaasa S, Aass N, Mastekaasa A, Lund E, Fossa SD (1991) Psychosocial well-being in testicular cancer patients. Eur J Cancer 27:1091–1095
31. Kiebert GM, de Haes JC, van de Velde CJ (1991) The impact of breast-conserving treatment and mastectomy on the quality of life of early-stage breast cancer patients: a review. J Clin Oncol 9:1059–1070
32. Lasry JC, Margolese RG, Poisson R, Shibata H, Fleischer D, Lafleur D, Legault S, Taillefer S (1987) Depression and body image following mastectomy and lumpectomy. J Chronic Dis 40:529–534
33. Maguire P (1992) Psychosocial well-being in testicular cancer patients. Eur J Cancer 28A:722
34. Meinardi MT, Gietema JA, van der Graaf WT, van Veldhuisen DJ, Runne MA, Sluiter WJ, de Vries EG, Willemse PB, Mulder NH, van den Berg MP, Koops HS, Sleijfer DT (2000) Cardiovascular morbidity in long-term survivors of metastatic testicular cancer. J Clin Oncol 18:1725–1732
35. Moynihan C (1987) Testicular cancer: the psychosocial problems of patients and their relatives. Cancer Surv 6:477–510
36. Nazareth I, Lewin J, King M (2001) Sexual dysfunction after treatment for testicular cancer. A systematic review. J Psychosom Res 51:735–743
37. Ozen H, Sahin A, Toklu C, Rastadoskouee M, Kilic C, Gogus A, Kendi S (1998) Psychosocial adjustment after testicular cancer treatment. J Urol 159:1947–1950
38. Richardson A (1998) Measuring fatigue in patients with cancer. Support Care Cancer 6:94–100
39. Rieker PP, Edbril SD, Garnick MB (1985) Curative testis cancer therapy: psychosocial sequelae. J Clin Oncol 3:1117–1126
40. Rieker PP, Fitzgerald EM, Kalish LA, Richie JP, Lederman GS, Edbril SD, Garnick MB (1989) Psychosocial factors, curative therapies, and behavioral outcomes. A comparison of testis cancer survivors and a control group of healthy men. Cancer 64:2399–2407
41. Rudberg L, Nilsson S, Wikblad K (2000) Health-related quality of life in survivors of testicular cancer 3 to 13 years after treatment. J Psychosoc Oncol 18:19–31
42. Rudberg L, Carlsson M, Nilsson S, Wikblad K (2002) Self-perceived physical, psychologic, and general symptoms in survivors of testicular cancer 3 to 13 years after treatment. Cancer Nurs 25:187–195
43. Sonneveld DJ, Hoekstra HJ, van der Graaf WT, Sluiter WJ, Mulder NH, Willemse PH, Koops HS, Sleijfer DT (2001) Improved long term survival of patients with metastatic nonseminomatous testicular germ cell carcinoma in relation to prognostic classification systems during the cisplatin era. Cancer 91:1304–1315
44. Sprangers MA, Schwartz CE (1999) Integrating response shift into health-related quality of life research: a theoretical model. Soc Sci Med 48:1507–1515
45. Stone P, Richards M, A'Hern R, Hardy J (2001) Fatigue in patients with cancers of the breast or rostate undergoing radical radiotherapy. J Pain Symptom Manage 22:1007–1015
46. Stuart NS, Grundy R, Woodroffe CM, Cullen MH (1990) Quality of life after treatment for testicular cancer–the patient's view. Eur J Cancer 26:291–294
47. Tamburini M, Filiberti A, Barbieri A, Zanoni F, Pizzocaro G, Barletta L, Ventafridda V (1989) Psychological aspects of testis cancer therapy: a prospective study. J Urol 142:1487–1489
48. Travis LB, Curtis RE, Storm H, Hall P, Holowaty E, Van Leeuwen FE, Kohler BA, Pukkala E, Lynch CF, Andersson M, Bergfeldt K, Clarke EA, Wiklund T, Stoter G, Gospodarowicz M, Sturgeon J, Fraumeni JF, Jr., Boice JD, Jr. (1997) Risk of second malignant neoplasms among long-term survivors of testicular cancer. J Natl Cancer Inst 89:1429–1439
49. van Basten JP, Jonker-Pool G, van Driel MF, Sleijfer DT, van de Wiel HB, Mensink HJ, Schraffordt-Koops H, Hoekstra HJ (1996) Fantasies and facts of the testes. Br J Urol 78:756–762
50. van 't Spijker A, Trijsburg RW, Duivenvoorden HJ (1997) Psychological sequelae of cancer diagnosis: a meta-analytical review of 58 studies after 1980. Psychosom Med 59:280–293
51. Wyatt G, Friedman LL (1996) Long-term female cancer survivors: quality of life issues and clinical implications. Cancer Nurs 19:1–7